

### **REMARKS**

Applicant acknowledges, with thanks, the shift of invention and the priority granted.

#### **Objections**

Fig2A shows that dMTase is inhibited by RNA since removing RNase an enzyme which degrades RNA (the -RNase lane) results in reduced activity relative to the activity seen in the Sephadex lane as indicated by reduced level of the C spot in the -RNase lane. The requirement for RNase for enhanced activity suggests that RNA inhibits the activity of the enzyme.

Fig 14B is an *in vitro* experiment. Purified demethylase from A549 cells was incubated with increasing concentrations of either the double stranded oligonucleotide [C<sup>m</sup>G C<sup>m</sup>G C<sup>m</sup>G]<sub>n</sub> = 20 inhibitor or a control {CG CG CG}<sub>n</sub> = 20 and demethylase activity *in vitro* was assayed using the volatile demethylation assay. In Fig. 14C the same reagents were used on living cells.

Claim 32 has been amended to delete reference to "or inhibitor" as suggested by the Examiner.

#### **Rejection under 35 U.S.C. §112, second paragraph**

The indefiniteness rejection of claims 32-34 and 41-44 has been rendered moot by limiting these claims to a method of altering demethylation activity as suggested by the Examiner.

The indefiniteness rejections of claims 32 and 42, and 32-34 have been rendered moot by limiting these claims to a method of altering demethylation activity in a cell as suggested by the Examiner.

**35 U.S.C. §101**

This rejection of claim 42 has been rendered moot by indirectly limiting this claim to a method of altering demethylation activity in a cell as suggested by the Examiner.

**Rejection under 35 U.S.C. §112, first paragraph**

Written Description

Claims 32, 42 and 44 were rejected as failing to comply with the written description requirement. The Office Action states that the claims are directed to a method to altering a demethylation activity of DNA demethylase by derivatives of imidazole while providing evidence for imidazole alone. As now amended, claim 32 no longer refers to derivatives of imidazole.

The Office Action also alleges that the specification does not teach that the antisense DNA inhibits the demethylating activity of DNA demethylase. Applicant respectfully disagrees as Figure 15 illustrates data using antisense DNA. Furthermore, the experiment and the results presented in Figure 15 are discussed in detail on page 43, lines 3 to 17. It is demonstrated that in the application that the antisense oligonucleotide (from an expression vector expressing the demethylase cDNA in the antisense orientation) reduces the levels of demethylase protein in the cell, thus reducing the availability of demethylation activity. It is also demonstrated that reducing demethylase protein leads to inhibition of cell growth on soft agar.

Applicant therefore respectfully submits that amended claim 32 and claim 42, satisfy the written description requirement in full compliance with the requirements of the first paragraph of 35 U.S.C. §112.

Claim 44 has been canceled, and the rejection of claim 44 failing the written description, has been thereby rendered moot.

Scope of enablement

Claims 32 and 44 also were rejected as not providing enablement for derivatives of imidazole. As now amended, claim 32 no longer refers to derivatives of imidazole and claim 44 has been canceled.

Applicant thus respectfully submits that, as amended, the claims of the application are properly enabled by the specification.

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

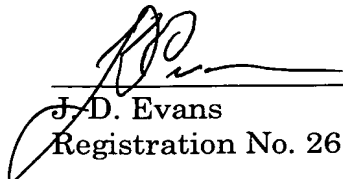
Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

If there are any questions regarding this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned at (202) 624-2845 so that such questions can be expeditiously resolved.

If necessary, this document should be construed as a Petition for an Extension of time sufficient to enable a timely response, and the Commissioner is hereby authorized to charge any needed fee to deposit account #05-1323 (Ref. 038630.48896US).

Respectfully submitted,

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J.D. Evans  
Registration No. 26,269

CROWELL & MORING LLP  
Intellectual Property Group  
P.O. Box 14300  
Washington, D.C. 20044-4300  
Telephone No.: (202) 624-2500  
Facsimile No.: (202) 628-8844  
JDE:moi